Supplementary data 1

Supplementary data Resource equation method

According to resource equation method:

$DF = N - k = kn - k = k(n - 1)$

The acceptable range of degrees of freedom (DF) for the error term in an analysis of variance (ANOVA) is between 10 to 20. Where N = total number of subjects, k = number of groups, and n = number of subjects per group.

By rearranging the formula, n is given as:

$n = DF/k + 1$

Based on the acceptable range of the DF, the DF in the formulas are replaced with the minimum (10) and maximum (20) DFs to obtain the minimum and maximum numbers of animals per group:

Minimum $n = 10/k + 1$

Maximum $n = 20/k + 1$

In this paper, the effects of ED-71 were compared between three groups (Sham, OVX, OVX+ED-71), the sample sizes per group are

Minimum $n = 10/3 + 1 = 4.3$ = rounded up to 5 animals/group

Maximum $n = 20/3 + 1 = 7.7$ = rounded down to 7 animals/group.

In conclusion, for the proposed study, between 5 and 7 animals per group are required. Our research used 5 rats (n=5) in each group, which is the sample size calculated according resource equation method.

Supplementary data 2

Supplementary data Bootstrapping to Figure 3

	Group	Mean	*P*
Day0 EphrinB2 mRNA	Control	1	<0.001*
	H_2O_2	0.6478633	
	H_2O_2+ED-71	0.7790294	<0.001**
Day3 EphrinB2 mRNA	Control	1	<0.001*
	H_2O_2	0.3239039	
	H_2O_2+ED-71	0.4840527	<0.001**
Day5 EphrinB2 mRNA	Control	1	<0.001*
	H_2O_2	0.5140316	
	H_2O_2+ED-71	0.7528643	<0.001**
Day7 EphrinB2 mRNA	Control	1	<0.001*
	H_2O_2	0.8299478	
	H_2O_2+ED-71	1.8367826	<0.001**
Day0 EphB4 mRNA	Control	1	<0.001*
	H_2O_2	0.4094953	
	H_2O_2+ED-71	0.8668878	<0.001**
Day3 EphB4 mRNA	Control	1	<0.001*
	H_2O_2	0.5654038	
	H_2O_2+ED-71	0.5276849	<0.001**
Day5 EphB4 mRNA	Control	1	<0.001*
	H_2O_2	0.5377046	
	H_2O_2+ED-71	0.8028877	<0.001**
Day7 EphB4 mRNA	Control	1	<0.001*
	H_2O_2	0.6358472	
	H_2O_2+ED-71	2.3071846	<0.001**
Day0 OPG mRNA	Control	1	<0.001*
	H_2O_2	0.4123206	
	H_2O_2+ED-71	0.8643591	<0.001**
Day3 OPG mRNA	Control	1	<0.001*
	H_2O_2	0.566477	
	H_2O_2+ED-71	0.527445	<0.001**
Day5 OPG mRNA	Control	1	<0.001*
	H_2O_2	0.537207	
	H_2O_2+ED-71	0.8030707	<0.001**
Day7 OPG mRNA	Control	1	<0.001*
	H_2O_2	0.6362562	
	H_2O_2+ED-71	2.3034438	<0.001**
Day0 RANKL mRNA	Control	1	<0.001*
	H_2O_2	2.606546	
	H_2O_2+ED-71	1.115029	<0.001**

Day3 RANKL mRNA	Control	1	<0.001*
	H_2O_2	6.098869	
	H_2O_2+ED-71	1.948132	<0.001**
Day5 RANKL mRNA	Control	1	<0.001*
	H_2O_2	2.976752	
	H_2O_2+ED-71	0.7560299	<0.001**
Day7 RANKL mRNA	Control	1	<0.001*
	H_2O_2	9.390473	
	H_2O_2+ED-71	1.585961	<0.001**
EphrinB2 protein	Control	0.9285611	<0.001*
	H_2O_2	0.5291064	
	H_2O_2+ED-71	0.9073277	<0.001**
EphB4 protein	Control	0.3503619	<0.001*
	H_2O_2	0.174954	
	H_2O_2+ED-71	0.3688031	<0.001**
OPG protein	Control	0.5401576	<0.001*
	H_2O_2	0.3792765	
	H_2O_2+ED-71	0.5984693	<0.001**
RANKL protein	Control	0.5105615	<0.001*
	H_2O_2	0.9186226	
	H_2O_2+ED-71	0.3506871	<0.001**
EphrinB2 fluorescence intensity	Control	1	<0.001*
	H_2O_2	0.5840272	
	H_2O_2+ED-71	1.2284489	<0.001**
EphB4 fluorescence intensity	Control	1	<0.001*
	H_2O_2	0.4186136	
	H_2O_2+ED-71	1.1356910	<0.001**

* Control vs. H_2O_2. ** H_2O_2 vs. H_2O_2+ED-71

Supplementary data 3

Supplementary data Bootstrapping to Figure 4

	Group	Mean	*P*
EphB4 mRNA	NC	1	
	ED-71+NC	1.607298	<0.001[#]
	SiEphB4	0.5004788	<0.001[##]
	ED-71 + SiEphB4	0.3346039	<0.001[###]
RANKL mRNA	NC	1	
	ED-71+NC	0.2233437	<0.001[#]
	SiEphB4	1.518018	<0.001[##]
	ED-71 + SiEphB4	1.4468368	<0.001[###]
OPG mRNA	NC	1	
	ED-71+NC	3.005825	<0.001[#]
	SiEphB4	0.3000667	<0.001[##]
	ED-71 + SiEphB4	0.9826686	<0.001[###]
OPG mRNA	NC	1	
	ED-71+NC	3.005825	<0.001[#]
	SiEphB4	0.3000667	<0.001[##]
	ED-71 + SiEphB4	0.9826686	<0.001[###]
EphB4 fluorescence intensity	NC	1	
	ED-71+NC	4.602377	<0.001[#]
	SiEphB4	0.4421483	<0.001[##]
	ED-71 + SiEphB4	0.6619803	<0.001[###]
EphB4 protein	NC	0.2818483	
	ED-71+NC	0.5567825	<0.001[#]
	SiEphB4	0.1661123	<0.001[##]
	ED-71 + SiEphB4	0.1832820	<0.001[###]
OPG protein	NC	0.4494232	
	ED-71+NC	0.8202374	<0.001[#]
	SiEphB4	0.3362976	<0.001[##]
	ED-71 + SiEphB4	0.3482290	<0.001[###]
RANKL protein	NC	0.3108056	
	ED-71+NC	0.1487850	<0.001[#]
	SiEphB4	0.7052066	<0.001[##]
	ED-71 + SiEphB4	0.5531208	<0.001[###]

[#] NC vs. ED-71+NC. [##] NC vs. SiEphB4. [###] ED-71+NC vs. ED-71 + SiEphB4

Supplementary data 4

Supplementary data Bootstrapping to Figure 5

	Group	Mean	*P*
MMP9 mRNA	Control	1	<0.001*
	H_2O_2	1.138819	
	H_2O_2+ED-71	0.2298798	<0.001**
Ctsk mRNA	Control	1	<0.001*
	H_2O_2	1.352797	
	H_2O_2+ED-71	1.077373	<0.001**
MMP9 protein	Control	0.5059425	<0.001*
	H_2O_2	0.7225320	
	H_2O_2+ED-71	0.3871974	<0.001**
Ctsk protein	Control	0.4866678	<0.001*
	H_2O_2	0.9745414	
	H_2O_2+ED-71	0.5326693	<0.001**
MMP9 mRNA	NC	1	<0.001$^{\#}$
	ED-71+NC	0.2270765	
	SiEphB4	2.216938	<0.00$^{\#\#}$
	ED-71 + SiEphB4	0.9930749	<0.001$^{\#\#\#}$
Ctsk mRNA	NC	1	<0.001$^{\#}$
	ED-71+NC	0.2943938	
	SiEphB4	3.017875	<0.00$^{\#\#}$
	ED-71 + SiEphB4	1.1990945	<0.001$^{\#\#\#}$
MMP9 protein	NC	0.5345529	<0.001$^{\#}$
	ED-71+NC	0.3196014	
	SiEphB4	0.9930331	<0.00$^{\#\#}$
	ED-71 + SiEphB4	0.6770321	<0.001$^{\#\#\#}$
Ctsk protein	NC	0.5623052	<0.001$^{\#}$
	ED-71+NC	0.2666358	
	SiEphB4	0.6435410	<0.00$^{\#\#}$
	ED-71 + SiEphB4	0.6876856	<0.001$^{\#\#\#}$

* Control vs. H_2O_2. ** H_2O_2 vs. H_2O_2+ED-71

$^{\#}$ NC vs. ED-71+NC. $^{\#\#}$ NC vs. SiEphB4. $^{\#\#\#}$ ED-71+NC vs. ED-71 + SiEphB4

Supplementary data 5

Supplementary data Bootstrapping to Figure 6

	Group	Mean	*P*
P-AKT protein	Control	0.5864814	<0.001*
	H_2O_2	0.2757692	
	H_2O_2+ED-71	0.7421448	<0.001**
P-PI3K protein	Control	0.4287305	<0.001*
	H_2O_2	0.1718247	
	H_2O_2+ED-71	0.3180476	<0.001**
P-AKT fluorescence intensity	Control	1	<0.001*
	H_2O_2	0.322442	
	H_2O_2+ED-71	0.7748974	<0.001**
P-PI3K fluorescence intensity	Control	1	<0.001*
	H_2O_2	0.2437001	
	H_2O_2+ED-71	1.0301669	<0.001**

* Control vs. H_2O_2. ** H_2O_2 vs. H_2O_2+ED-71

Supplementary data 6

Supplementary data Bootstrapping to Figure 7

	Group	Mean	*P*
P-AKT fluorescence intensity	NC	1	
	ED-71+NC	2.565105	<0.001#
	SiEphB4	0.3721746	<0.001##
	ED-71 + SiEphB4	0.3627714	<0.001###
P-PI3K fluorescence intensity	NC	1	
	ED-71+NC	1.882617	<0.001#
	SiEphB4	0.3729393	<0.001##
	ED-71 + SiEphB4	0.3660938	<0.001###
P-AKT protein	NC	0.5335103	
	ED-71+NC	0.7991396	<0.001#
	SiEphB4	0.1700419	<0.001##
	ED-71 + SiEphB4	0.2172040	<0.001###
P-PI3K protein	NC	0.5523302	
	ED-71+NC	0.8012697	<0.001#
	SiEphB4	0.3112832	<0.001##
	ED-71 + SiEphB4	0.2537139	<0.001###
P-AKT protein	H_2O_2	0.3430358	
	H_2O_2+ LY294002	0.1566890	<0.001&
	H_2O_2 + ED-71	0.5776687	<0.001&&
	H_2O_2 + ED-71+ LY294002	0.1959548	<0.001&&&
P-PI3K protein	H_2O_2	0.3130758	
	H_2O_2+ LY294002	0.1856422	<0.001&
	H_2O_2 + ED-71	0.7096350	<0.001&&
	H_2O_2 + ED-71+ LY294002	0.3134323	<0.001&&&
RANKL protein	H_2O_2	0.3967519	
	H_2O_2+ LY294002	0.6286984	<0.001&
	H_2O_2 + ED-71	0.2075843	<0.001&&
	H_2O_2 + ED-71+ LY294002	0.6227701	<0.001&&&
OPG protein	H_2O_2	0.5427796	
	H_2O_2+ LY294002	0.1141555	<0.001&
	H_2O_2 + ED-71	0.8477257	<0.001&&
	H_2O_2 + ED-71+ LY294002	0.3330063	<0.001&&&
P-AKT protein	H_2O_2	0.6306323	<0.001^
	H_2O_2+ ARQ092	0.3526867	
	H_2O_2 + ED-71	1.1937543	<0.001^^

	H_2O_2 + ED-71+ ARQ092	0.5350711	<0.001^^^
	H_2O_2	0.2385276	<0.001^
	H_2O_2+ ARQ092	0.4038239	
RANKL protein	H_2O_2 + ED-71	0.1090362	<0.001^^
	H_2O_2 + ED-71+ ARQ092	0.4512656	<0.001^^^
	H_2O_2	0.4397608	<0.001^
	H_2O_2+ ARQ092	0.2009165	
OPG protein	H_2O_2 + ED-71	0.8377941	<0.001^^
	H_2O_2 + ED-71+ ARQ092	0.3734085	<0.001^^^

NC vs. ED-71+NC. ## NC vs. SiEphB4. ### ED-71+NC vs. ED-71 + SiEphB4

& H_2O_2 vs. H_2O_2+ LY294002. && H_2O_2 vs. H_2O_2 + ED-71.

&&& H_2O_2+ LY294002 vs. H_2O_2 + ED-71+ LY294002

^ H_2O_2 vs. H_2O_2+ ARQ092. ^^ H_2O_2 vs. H_2O_2 + ED-71.

^^^ H_2O_2+ ARQ092 vs. H_2O_2 + ED-71+ ARQ092